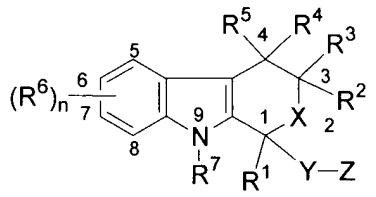
Claims

1. A therapeutic method for treatment of non-malignant diseases characterized by the excessive growth of tissue comprising administering to a patient in need of said therapy, an effective amount of a compound of formula (I):



(I)

wherein R^1 is lower alkyl, (hydroxy)lower alkyl, lower alkenyl, lower alkynyl, lower cycloalkyl, phenyl, benzyl or 2-thienyl;

R^2, R^3, R^4 and R^5 are the same or different and are each hydrogen or lower alkyl;

each R^6 is independently hydrogen, lower alkyl, hydroxy, (hydroxy)lower alkyl, lower alkoxy, benzyloxy, lower alkanoyloxy, nitro or halo;

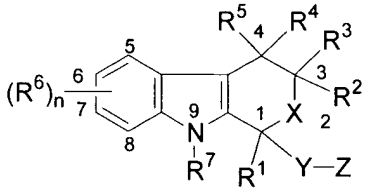
R^7 is hydrogen, lower alkyl or lower alkenyl, X is oxy and thio, Y is carbonyl, -(C_1-C_3)alkyl(CO)-, -$(CH_2)_{1-3}$-, or -$(CH_2)_{1-3}SO_2$-;

Z is hydroxy, lower alkoxy, (C_2-C_4)acyloxy, -N(R^8)(R^9), phenylamino, (ω-(4-pyridyl)(C_2-C_4 alkoxy), (ω-((R^8)(R^9) amino)(C_2-C_4 alkoxy), an amino acid ester of (ω-(HO)(C_2-C_4))alkoxy, -N(R^8)CH(R^8)CO_2H, 1′-D-glucuronyloxy, -SO_3H, -PO_4H_2, -N(NO)(OH), -SO_2NH_2, -PO(OH)(NH_2), -$OCH_2CH_2N(CH_3)_3^+$, or tetrazolyl;

wherein R^8 and R^9 are each H, (C_1-C_3)alkyl or together with N are a 5- or 6-membered heterocyclic ring comprising 1-3 N(R^8), S or nonperoxide O; n is 0, 1, 2, or 3; and

each alkyl or phenyl group of R^1, R^2, R^3, R^4, R^5, R^6, R^7 and Z is optionally substituted with 1, 2, or 3 $(C_1\text{-}C_4)$alkyl groups; or a pharmaceutically acceptable salt thereof.

2. A therapeutic method for treatment of mammalian hyperplastic cells comprising administering to a patient in need of said therapy a chemotherapeutic agent in combination with an effective amount of a compound of formula (I):



(I)

wherein R^1 is lower alkyl, (hydroxy)lower alkyl, lower alkenyl, lower alkynyl, lower cycloalkyl, phenyl, benzyl or 2-thienyl;

R^2, R^3, R^4 and R^5 are the same or different and are each hydrogen or lower alkyl;

each R^6 is independently hydrogen, lower alkyl, hydroxy, (hydroxy)lower alkyl, lower alkoxy, benzyloxy, lower alkanoyloxy, nitro or halo; and n is 1-3;

R^7 is hydrogen, lower alkyl or lower alkenyl, X is oxy and thio, Y is carbonyl, $-(C_1.C_3)$alkyl(CO)-, $-(CH_2)_{1\text{-}3}$-, or $-(CH_2)_{1\text{-}3}SO_2$-;

Z is hydroxy, lower alkoxy, $(C_2\text{-}C_4)$acyloxy, $-N(R^8)(R^9)$, phenylamino, (ω-(4-pyridyl)$(C_2\text{-}C_4$ alkoxy), (ω-($(R^8)(R^9)$ amino)$(C_2\text{-}C_4$ alkoxy), an amino acid ester of (ω-(HO)$(C_2\text{-}C_4)$)alkoxy, $-N(R^8)CH(R^8)CO_2H$, 1′-D-glucuronyloxy, $-SO_3H$, $-PO_4H_2$, -N(NO)(OH), $-SO_2NH_2$, -PO(OH)(NH_2), $-OCH_2CH_2N(CH_3)^{3+}$, or tetrazolyl;

wherein R^8 and R^9 are each H, $(C_1\text{-}C_3)$alkyl or together with N are a 5- or 6-membered heterocyclic ring comprising 1-3 $N(R^8)$, S or nonperoxide O;

wherein each alkyl or phenyl group of R^1, R^2, R^3, R^4, R^5, R^6, R^7 and Z is optionally substituted with 1, 2, or 3 $(C_1\text{-}C_4)$alkyl groups; or a pharmaceutically acceptable salt thereof.

3. The method of claim 1 or 2, wherein the disease is benign prostate hyperplasia, fibroplastic dysplasia of the breast, fibroplastic growth in the uterus or fibroplastic growth in the cervix.

4. The method of claim 3, wherein the disease is benign prostate hyperplasia.

5. The method of claim 3, wherein the disease is fibroplastic dysplasia of the breast, fibroplastic growth in the uterus or fibroplastic growth in the cervix.

6. The method of claim 3, wherein the compound of formula (I) is administered orally.

7. The method of claim 2, wherein the compound of formula (I) is administered in combination with an androgen inhibitor, or an α-1 adrenergic receptor blocker.

8. The method of claim 7, wherein the androgen inhibitor is finasteride.

9. The method of claim 7, wherein the α-1 adrenergic receptor blockers is phenoxybenzamine, prozosin, terazin, doxazosin, or tamsulosin.

10. The method of claim 3, wherein Z is the L-valine or L-glycine ester of 2-hydroxyethoxy.

11. The method of claim 3, wherein Z is N-morpholinoethoxy.

12. The method of claim 3, wherein each R^8 is H, CH_3 or i-Pr.

13. The method of claim 3, wherein Z is $OCH_2CH_2N(CH_3)_3$.

14. The method of claim 3, wherein the compound of formula (I) is etodolac.

15. The method of claim 3, wherein the compound of formula (I) is the R(-)isomer.